4-(METHYLNITROSAMINO)-1-(3-PYRIDYL)-1-BUTANONE (NNK)

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CAS No.: 64091-91-4
Chem. Abstr. Name: 1-Butanone, 4-(methylnitrosoamino)-1-(3-pyridinyl)-

5. Summary of Data Reported and Evaluation

5.1 Exposures

4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) has been found in a variety of tobacco products (chewing tobacco, snuff, cigarettes and cigars), in mainstream and sidestream smoke from cigars and cigarettes, in saliva of chewers of betel quid with tobacco, and in saliva of oral-snuff users. Some of the NNK in saliva appears to be formed endogenously from salivary nitrite and nicotine. Thus, there is widespread exposure to NNK among users of tobacco products and those exposed to sidestream smoke.

5.2 Experimental data

NNK was tested for carcinogenicity in several studies by subcutaneous injection in rats and hamsters and by intraperitoneal injection in mice. In rats, it induced carcinomas of the nasal cavity, lung and liver, with a clear dose-response relationship. In hamsters, it induced benign and malignant tumours of the nasal cavity, trachea and lung, even after a single administration. In mice, NNK and its metabolites 4-(methylnitrosamino)-1-(3-pyridyl-*N*-oxide)-1-butanone and 4-(methylnitrosamino)-1-(3-pyridyl)butan-1-ol induced benign and malignant tumours of the lung.

NNK and its metabolites can cross the placental barrier in mice. NNK can be metabolically activated by mouse foetal tissues.

Administration of NNK to rats results in abnormal DNA methylation in liver and lung. NNK is mutagenic to *Salmonella typhimurium* in the presence of an exogenous metabolic system. It induces unscheduled DNA synthesis in primary cultures of rat hepatocytes.

5.3 Human data

No case report or epidemiological study of the carcinogenicity of NNK to humans was available to the Working Group.

5.4 Evaluation

There is *sufficient evidence* for the carcinogenicity of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone to experimental animals.

No data on humans were available.

For definition of the italicized terms, see Preamble Evaluation.

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Subsequent evaluation: Suppl. 7 (1987) (p. 68: **Group 2B**)

Synonym

- 4-(*N*-Methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone

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